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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,097	02/21/2002	Kevin J. Rozeboom	066379-9001	2833

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,097	ROZEBOOM ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-9,11-13,15 and 17-53* is/are pending in the application.

4a) Of the above claim(s) *19-22,33-47 and 50-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-9,11-13,15,17,18,23-32,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 1-9, 11-13, 15, 17, 18, 23-32, 48 and 49 as amended [11/24/2003] are under examination in the instant office action.

Claims 10, 14 and 16 are canceled by applicants [11/24/2003]. Claims 19-22, 33-47 and 50-53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, 7, 11-13, 15, 17, 32 and 49 as amended are rejected under 35 U.S.C. 102(b) as being anticipated by Naz et al. in the light of evidence by Lackey et al. and in the light of evidence by Nocera et al.

Claims 1, 2, 7, 11-13, 15, 17 as amended are now directed to a composition comprising 3 major components that are 1) a reproductive cell and a medium,

wherein the medium comprises two growth factors that are

2) insulin-like growth factor (IGF) and

3) transforming growth factor (TGF).

Some claims are further drawn to the reproductive cell that is mammalian or human sperm cell. Some claims are further drawn to the presence of TGF beta 1, TGF beta 2 and IGF-1 in the medium. Claim 32 is further drawn to the presence of cryopreservative in the medium or in the composition. Claim 49 is drawn to a composition with TGF beta 1, TGF beta 2 and IGF-1.

The reference by Naz et al. discloses spermatozoa samples that are collected from donors of proven fertility (page 157, col. 1, lines 7-8). Before further centrifugation and dilution these collected samples contain sperm cell(s) (component 1) and seminal plasma (medium) containing IGF (component 2) and TGF (component 3). The fact that mammalian or human seminal plasma contains IGF-1 is evidenced by Lackey et al. (see page 116, par. 3, last line). The fact that mammalian or human seminal plasma contains TGF beta 1 and TGF beta 2 is evidenced by Nocera et al. (abstract).

Thus, the collected semen samples or semen ejaculates are compositions identical to the composition of the instant claims 1, 2, 7, 11-13, 15 and 17.

The seminal plasma contains plasma proteins and, thus, it is considered to comprise a generic cryopreservative within the meaning of the claim 32.

Although the use of the composition of claim 49 is intended for porcine cells, the claim 49 does not require the presence of any cells. Thus, claim 49 is also anticipated by the cited collected sample that contains mammalian seminal plasma.

Claims 1, 2, 7, 11-13, 15, 17, 29, 32, 48 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Ovesen et al. {Fertility and Sterility. 1995, Vol. 63, No. 4, pages 913-918} in the light of evidence by Nocera et al. and in the light of evidence by US 4,156,427.

Claims 1, 2, 7, 11-13, 15, 17, 32 and 49 as explained above.

Claim 29 is further drawn to concentration of IGF-1 that is from 0.1 ng/L to 30 μg/L. Claim 48 is further drawn to the presence of zinc.

Ovesèn et al. discloses collected semen samples or ejaculates that contain human sperm cells and human seminal plasma. The reference teaches that concentration of IGF-1 in the samples with human sperm cells and human seminal plasma is 18 μg/L (abstract).

The fact that mammalian or human seminal plasma contain TGF beta 1 and TGF beta 2 is evidenced by Nocera et al. (abstract). The seminal plasma contains plasma proteins and, thus, it is considered to comprise a generic cryopreservative within the meaning of the claim 32. The fact that human seminal plasma contains zinc is evidenced by US 4,156,427 (col. 1, line 38).

Thus, the collected semen samples or semen ejaculates are compositions identical to the composition of the instant claims 1, 2, 7, 11-13, 15, 19, 29, 32 and 48.

Although the use of the composition of claim 49 is intended for porcine cells, the claim 49 does not require the presence of any cells. Thus, claim 49 is also anticipated by the cited collected sample that contains mammalian seminal plasma.

Claim Rejections - 35 USC § 102/103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-9, 11-13, 15, 17, 18, 29, 32, 48 and 49 are rejected under 35 U.S.C. 102(b) as anticipated by Ovesen et al. in the light of evidence by Nocera et al. and in the light of evidence by US 4,156,427, or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ovesen et al. taken with Nocera et al., US 4,156,427, Gerfen et al. {Theriogenology, 1994, 41:461-469} and Vardinon et al. {Human Reproduction, 1990, Vol. 5, No. 3, pages 294-297}.

Claims 1, 2, 7, 11-13, 15, 17, 29, 32, 48 and 49 as explained above. Claims 3-6, 8 and 9 are further drawn to sperm cells of various animals in the composition with the medium. Some

claims are further drawn to various concentrations of growth factors, to the presence of transferrin, inositol, and fructose in the medium.

The reference by Ovesen discloses a composition of the collected semen ejaculates comprising animal sperm cells and animal seminal plasma medium with growth factors including of TGF beta 1, TGF beta 2 and IGF-1 in the light of teaching by Nocera et al as explained above. The seminal plasma contains plasma proteins and, thus, it is considered to comprise a generic cryopreservative within the meaning of the claim 32. The fact that human seminal plasma contains zinc is evidenced by US 4,156,427 (col. 1, line 38).

Although the reference by Ovesen is silent about the presence of transferrin, inositol and fructose in the seminal plasma of the sperm sample, the reference by Gerfen et al. demonstrates that animal or boar seminal plasma contains fructose and inositol (see abstract) and the reference by Vardinon et al. demonstrates that animal or human seminal plasma contains transferrin (abstract).

Thus, the cited reference by Ovesen et al. discloses a composition that is identical to the presently claimed composition since it contains animal or human sperm cells and animal or human seminal plasma with factors and ingredients as the claimed composition (claims 1, 2, 7, 11-13, 15, 17, 18, 29, 32, 48 and 49). In the alternative, even if the claimed composition is not identical to the composition with regard to a particular animal, there is a reasonable believe that the semen samples collected from the various animals that are claimed would inherently contains sperm cells and seminal plasma with factors and ingredients that are claimed since it has established that animal seminal plasma contains TGF beta 1, TGF beta 2, IGF-1, transferrin, inositol, fructose and zinc as adequately demonstrated by the cited references {US 4,156,427;

Nocera et al., Gerfen et al. and Vardinon et al.}. Thus, the claimed compositions as drawn to various animals (claims 2-9) would have been obvious to those skilled in the art within the meaning of USC 103.

Furthermore, although in the semen sample composition of the reference by Ovesen the particular concentrations of growth factors, for example: IGF-1, appears to be at the upper level as compared to the presently claimed compositions, the semen samples are diluted during storage and/or further manipulations, and, thus, theirs concentrations would obviously fall within at least some of the lower ranges that are presently claimed. Although in the semen sample composition of the reference by Ovesen contain higher amounts of TGF factors in the light of Nocera et al. as compared to the presently claimed compositions, the semen samples are diluted during storage and/or further manipulations, and, thus, theirs concentrations would obviously fall within at least some the lower ranges that are presently claimed. Although the reference by Ovesen teaches human seminal plasma, and, thus, it is silent with respect to the seminal plasma of all various animals that are claimed, the amounts of growth factors and other ingredients are obviously would be variable with respect to particular animals and/or upon further semen sample dilutions and manipulations.

Therefore, even if the claimed compositions, each comprising particular animal cells and corresponding animal seminal plasma, are not identical to the referenced Ovesen's semen sample composition with regard to the particular animals and, thus, particular amounts of the inherently present growth factors in the animal seminal plasma, the differences between the semen sample compositions would have been obvious to those skilled in the art within the meaning of USC 103 as applied to different animals and/or as applied to the obviously possible dilutions during semen

samples manipulations. The cited references US 4,156,427, Nocera et al., Gerfen et al. and Vardinon et al. adequately demonstrate that animal seminal plasma contains TGF beta 1, TGF beta 2, IGF-1, transferrin, fructose, inositol and zinc.

Accordingly, the claimed invention, drawn to a composition comprising sperm cell(s) and generic media with factors/ingredients found in animal seminal plasma, as a whole was at least prima facie obvious, if not anticipated by the Ovesen's reference, especially in the absence of evidence to the contrary.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-9, 11-13, 15, 17, 18, 23-32, 48 and 49 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over the reference by Naz et al. and the reference by Lackey et al. taken with ATCC Catalogue, US patent 6,140,121 [IDS reference AD], US 6,150,163 and reference by Nocera et al.

Claims are directed to a cell culture medium composition comprising reproductive cell(s) and two growth factors IGF and TGF. The cell culture medium is intended for various animal sperm cells. Some claims are further drawn to the use of TGF beta 1, TGF beta 2 and IGF-1 in the culture medium. Some claims are further drawn to the use of TGF beta 1 at concentration from about 0.1 ng/L to about 10 μg/L in the culture medium, to the use of TGF beta 2 concentration from about 0.1 ng/L to about 200 ng/L in the cell culture medium and to the use of IGF-1 at concentration from about 0.1 ng/L to about 30 μg/L in the cell culture medium. Some claims are further drawn to incorporation of inositol or transferrin or fructose in the cell culture

medium. Some claims are further drawn to incorporation of cryopreservative in the culture medium. Some claims are further drawn to incorporation of zinc in the culture medium.

In this instant rejection all cited references are relied upon as explained in the prior office action and repeated herein below for the disclosure of animal sperm cell culture media. The cited references also teach incorporation of animal sperm cells into the media as encompassed by the instant claims as amended.

The reference by Naz et al. and by Lackey et al. are relied upon as explained above for the disclosure of animal sperm cell culture media with at least one growth factor TGF beta or IGF-1 in view of the disclosure by the ATCC Catalogue which provides evidence related to the presence of zinc and inositol in the regular basal animal cell culture media. In addition, US 6,140,121 is relied upon to demonstrate that animal sperm cell culture media comprise basal media or balanced salt solutions, growth factors and other sperm stimulants, supplements and additives (col. 15, line 1 and lines 53-67) suitable for sperm cells of various animal including humans, avians or exotic species (col. 4, lines 50-52).

The compositions of both cited references by Naz et al. and by Lackey et al. comprise various cryoprotective agents. But they are missing disclosure related to the use of fructose as cryoprotective agent. However, the cited US 6,140,121 teaches the use of fructose in compositions intended for freezing animal sperm cells, for example: see col. 26, lines 44-49, as well as other cryoprotective agents including serum albumin, amino acids and sugars (see paragraph bridging col.16 and col. 17) that are disclosed by references by Naz et al. and by Lackey et al.

The cited references by Naz et al. and by Lackey et al are silent with regard to transferrin in basal culture media. However, the cited patent US 6,150,163 teaches incorporation of transferrin supplement into basal animal cell culture media with growth factor(s) (table 1).

Both cited references by Naz et al. and by Lackey et al. disclose concentrations of at least one growth factor in sperm culture media that are within the presently claimed ranges. In particular, the reference by Naz et al. teaches incorporation of growth factor TGF beta 1 into sperm cell culture medium but it is silent with regard to growth factor IGF. However, the reference by Lackey et al teaches incorporation of IGF-1 into animal sperm cell culture medium. Further, the reference by Lackey et al also teaches that growth factors including IGF are within animal seminal plasma or a natural environment for animal sperm cells. In addition, the reference by Nocera et al. teaches that other growth factors including TGF beta 1 and TGF beta 2 are also within animal seminal plasma.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to combine growth factors including IGF-1, TGF beta 1 and TGF beta 2 in an animal sperm cell culture medium with a reasonable expectation of success in providing a physiologically suitable medium for sperm cells of various animals because the physiologically suitable conditions provided by seminal plasma include growth factors that are presently claimed and because the prior art teaches incorporation of growth factors TGF beta and IGF into artificial cell culture media intended for sperm cells. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary. It is well known that it is *prima facie* obvious to combine ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful

for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). Further, it is considered to be within the purview of ordinary skill practitioner to adjust concentrations of particular growth factors and/or other ingredients with regard to a particular application intended for sperm cells for the expected benefit in maximizing sperm viability and/or optimizing sperm survival, preservation and/or fertility.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Some of the applicants' arguments filed 11/24/2003 as related to the claim rejection under 35 U.S.C. 102(b) with respect to claims as amended have been considered but are moot in view of the new ground(s) of rejection.

Claim rejections under 35 U.S.C. 103(a) as being unpatentable over US 6,150,163 alone has been withdrawn because the disclosure of this patent as a whole is not related to the reproductive cells or sperm cells. However, it teaches nutrient supplements in the basal animal cell culture medium.

Other applicants' arguments filed 11/24/2003 (page 10) have been fully considered but they are not found persuasive.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on

obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

With respect to the reference by Naz et al. applicants argue that it does not provide any motivation to use TGF because its addition to the sperm medium has no effect on sperm motility. However, the cited reference teaches another benefit of the TGF such as enhanced expression of proteins that are regarded as important for proper sperm development and new protein synthesis (abstract or page 162, col. 2). Moreover, the claimed invention is not a method for increasing sperm motility but a sperm-containing composition.

Upon review of the cited reference by Lackey et al. applicants' argument about sperm motility is not found true. This reference clearly states the fact and the benefit of the increased sperm motility as result of addition of IGF-I into the sperm-containing composition (abstract or page 119. first line at section "Discussion").

Applicants appear to argue that there is no suggestion to combine references. However all cited references are in the same field of endeavor (that is sperm cell culture media including basal animal cell culture medium ingredients) and seek to solve the same problems as the instant application and claims (such as to provide a sperm cell culture medium, for example), and one of skill in the art is free to select components available in the prior art. In re Winslow, 151 USPQ 48 (CCPA, 1966). Therefore, the applicants' allegations that the cited references have any

purpose and, thus, office action is lacking expectation of success and motivation in providing a sperm cell containing composition or culture media with both growth factors, are not true.

Thus, applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Vera Afremova

AU 1651

February 18, 2004

VERA AFREMOVA

PATENT EXAMINER